FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE' ENTERED AT 14:08:04 ON 24 MAY 2005

L1 5 S CAALR1
L2 123 S ALR1
L3 28 S L2 (S) (YEAST OR CEREVISIAE OR ALBICANS)
L4 2 DUP REM L1 (3 DUPLICATES REMOVED)
L5 11 DUP REM L3 (17 DUPLICATES REMOVED)
L6 0 S L2 (S) CANDIDA

IN Carr, Grant J.; Xu, Howard H.; Foulkes, Gordon J.; Zamudio, Carlos; Haselbeck, Robert; Ohlsen, Kari L.; Zyskind, Judith W.; Wall, Daniel; Trawick, John D.; Yamamoto, Robert T.; Roemer, Terry; Jiang, Bo; Boone, Charles; Bussey, Howard
SO PCT Int. Appl., 640 pp.
CODEN: PIXXD2
TI Methods for identifying the target of a compound which inhibits cellular proliferation
AB The invention relates to cultures or collections of strains which overexpress or underexpress gene products required for the proliferation of an organism. The invention also includes methods for identifying the target on which a compd. which inhibits the proliferation of an organism acts and methods for identifying the extent to which a strain is present in a culture or collection of strains. Thus, a culture is obtained comrpising a plurality of strains wherein each strain overexpresses a different gene product which is essential for prolifeation. The culture is contacted with a sufficient concn. of an agent to inhibit th eproliferation of strains which do not overexpress the gene product on which the agent acts, such that strains which overexpress the gene product on which the agent acts proliferate more rapidly than strains which do not overexpress said gene product on which the agent acts. The gene product which is overexpressed in a strain which proliferates more rapidly in the culture is then identified. Expression levels of gene transcripts are detd. using hybridization and/or amplification methods std. to the art. Genes required for cellular proliferation of microbial organisms are identified by antisense RNA technol. Nucleotide sequences are provided for nucleic acid fragments whose expression results in detrimental effects on proliferation of Escherichia coli, Staphylococcus aureus, Salmonella typhimurium, Klebsiella pneumoniae, Pseudomonas aeruginosa, or Enterococcus faecalis. [This abstr. record is one of three records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

IN Roemer, Terry; Bussey, Howard; Davison, John
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
TI Protein and DNA sequences of Candida albicans essential fungal specific genes and use thereof in antifungal drug discovery
AB The invention relates to the identification and disruption of essential fungal specific genes isolated in the yeast pathogen Candida albicans namely CaKRE5, CaALR1 and CaCDC24 and to the use thereof in antifungal diagnosis and as essential antifungal targets in a fungal species for antifungal drug discovery. More specifically, the invention relates to the CaKRE5, CaALR1 and CaCDC24 genes, to their use to screen for antifungal compds. and to the drugs identified by such.

IN Gardner, Richard Clague; Macdiarmid, Colin Whiti; Hay, Robert John Mouat
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
TI Aluminum resistance genes from Saccharomyces cerevisiae
AB A method of isolating genes conferring resistance to aluminum is provided and two particular aluminum tolerant genes (ALR1 and ALR2) are described. The Saccharomyces cerevisiae strains SH2332 and CG379 differ in their basal Al tolerance in LPM medium, and were used to select for plasmids which allow growth on inhibitory concns. of aluminum, and the genes were isolated by by mapping, deletion construction, and PCR. Partial sequencing identified ALR1 and ALR2 as open reading frames in the known genome sequence (nucleotides 416-2995 in GenBank Accession No. U41293 and nucleotides 33,272-35,848 in GenBank D44603, resp.). The 2 tolerance genes were isolated from yeast strains but were found to have homol. with bacterial genes responsible for divalent ion uptake. Both genes give

resistance to Al and to Ga, and make yeast cells sensitive to a range of other metals, including Zn, Co, Mn, Ni, La, and Sc. The gene products apparently transport Mg, Ni, Co, Zn, Mn, Sc, and La into the cell, and Al and Ga inhibit this transport. Hence, a method of isolating divalent cation transporters is envisaged by using complementation of magnesium transporter mutant strains of yeasts aluminum tolerance genes. The genes can be used in recombinant nucleic acid systems to treat cation toxicities, esp. Al and Mn toxicity.

AU MacDiarmid C W; Gardner R C
SO Journal of biological chemistry, (1998 Jan 16) 273 (3) 1727-32.
Journal code: 2985121R. ISSN: 0021-9258.
TI Overexpression of the Saccharomyces cerevisiae magnesium transport system confers resistance to aluminum ion.
AB Ionic aluminum (Al3+) is toxic to plants, microbes, fish, and animals, but the mechanism of its toxicity is unknown. We describe the isolation of two yeast genes (ALR1 and ALR2) which confer increased tolerance to Al3+ and Ga3+ ions when overexpressed while increasing strain sensitivity to Zn2+, Mn2+, Ni2+, Cu2+, Ca2+, and La3+ ions. The Alr proteins are homologous to the Salmonella typhimurium CorA protein, a bacterial Mg2+ and Co2+ transport system located in the periplasmic membrane. Yeast strains lacking ALR gene activity required additional Mg2+ for growth, and expression of either ALR1 or ALR2 corrected the Mg(2+)-requiring phenotype. The results suggest that the ALR genes encode the yeast uptake system for Mg2+ and other divalent cations. This hypothesis was supported by evidence that 57Co2+ accumulation was elevated in ALR-overexpressing strains and reduced in strains lacking ALR expression. ALR overexpression also overcame the inhibition of Co2+ uptake by Al3+ ions. The results indicate that aluminum toxicity to yeast occurs as a consequence of reduced Mg2+ influx via the Alr proteins. The molecular identification of the yeast Mg2+ transport system should lead to a better understanding of the regulation of Mg2+ homeostasis in eukaryote cells.

AU Graschopf A; Stadler J A; Hoellerer M K; Eder S; Sieghardt M; Kohlwein S D; Schweyen R J
SO Journal of biological chemistry, (2001 May 11) 276 (19) 16216-22.
Electronic Publication: 2001-02-20.
Journal code: 2985121R. ISSN: 0021-9258.
TI The yeast plasma membrane protein Alr1 controls Mg2+ homeostasis and is subject to Mg2+-dependent control of its synthesis and degradation.
AB The Saccharomyces cerevisiae ALR1 (YOL130w) gene product Alr1p is the first known candidate for a Mg(2+) transport system in eukaryotic cells and is distantly related to the bacterial CorA Mg(2+) transporter family. Here we provide the first experimental evidence for the location of Alr1p in the yeast plasma membrane and for the tight control of its expression and turnover by Mg(2+). Using well characterized npi1 and end3 mutants deficient in the endocytic pathway, we demonstrate that Alr1 protein turnover is dependent on ubiquitination and endocytosis. Furthermore, cells lacking the vacuolar protease Pep4p accumulated Alr1p in the vacuole. Mutants lacking Alr1p (Deltaalr1) showed a 60% reduction of total intracellular Mg(2+) compared with the wild type and failed to grow in standard media. When starved of Mg(2+), mutant and wild-type cells had similar low levels of intracellular Mg(2+); but upon addition of Mg(2+), wild-type cells replenished the intracellular Mg(2+) pool within a few hours, whereas Deltaalr1 mutant cells did not. Expression of the bacterial Mg(2+) transporter CorA in the yeast Deltaalr1 mutant partially restored growth in standard media. The results are discussed in terms of Alr1p being a plasma membrane transporter with high selectivity for Mg(2+).